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The Utilization of Stellate Ganglion Block in the Treatment of Long-COVID: A Case Series

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Background: With the recent COVID-19 pandemic, chronic pain physicians undoubtedly face the challenge of treating long-COVID within the already complex chronic pain patient population. Sympathetic blockade of the stellate ganglion has historically been utilized as a diagnostic and therapeutic tool in confirming and targeting the sympathetically mediated component of many chronic pain conditions, but its role in treating long-COVID symptoms has yet to be thoroughly studied or elucidated.

Case Series: We present a unique case series where the utilization of stellate ganglion blockade in one case and use of stellate ganglion blockade followed by rhizotomy in another were successful in sustained and near-complete relief of all initial long-COVID symptoms during a 3-month follow-up period.

Conclusions: Our case series presents promising results on the role of stellate ganglion blockade in the sustained and near-complete relief of multiple long-COVID symptoms during the longest known follow-up period to date.

Key words: COVID-19, dysautonomia, long-COVID, rhizotomy, stellate ganglion block

BACKGROUND

The recent COVID-19 pandemic has caused a devastating toll on human life. With over half a billion people globally who have survived infection, the long-term impacts resulting from COVID-19 remain unclear and are often overlooked.

The term "long-COVID" describes the persistent symptoms after primary infection of the SARS-CoV-2 virus such as fatigue, dizziness, difficulty thinking or concentrating, headache, sleep problems, smell and taste disturbances, respiratory symptoms such as dyspnea and cough, cardiac dysrhythmias, postural orthostatic tachycardia syndrome, gastrointestinal disturbances, musculoskeletal pain, and more (1,2).

With recently published Centers for Disease Control and Prevention data showing that 25% or more of individuals aged 18 years and older will experience long-COVID symptoms, chronic pain physicians undoubtedly face the challenge of treating long-COVID within the already complex chronic pain patient population (2). The current treatments for long-COVID are limited, mainly focused on symptom-targeted therapy and rehabilitation, vitamin and electrolyte supplementation when indicated, and holistic support (3). One can thus imagine the debilitating toll of long-COVID on patients whose symptoms are refractory to the currently limited available treatments.

Of specific interest to interventional pain physicians on the topic of treating long-COVID is the role of the stellate ganglion, which has historically been utilized as a diagnostic tool in confirming the sympathetically mediated component of chronic conditions; however,

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its role in treating long-COVID symptoms has yet to be thoroughly studied or elucidated.

Liu et al (4) suggested stellate ganglion block (SGB) as a novel treatment in long-term COVID symptoms due to aberrant network adaptation because of a sympathetic/parasympathetic imbalance implicating dysautonomia in the pathophysiology of long-term COVID. Those authors reported sustained positive clinical outcomes in 2 long-COVID patients after treatment with SGB. Our current case report is the first case series with a longer follow-up (3 months vs 2 months in Liu et al), the first rhizotomy reported in a patient for this condition, and the first case series focusing on the 10 most common long-COVID symptoms.

CASES

Patient 1

A 55-year-old man with a past medical history of obesity, hypertension, and type-2 diabetes presented to the clinic with multiple long-COVID symptoms that began 4 months after initially testing positive for COVID-19. These symptoms included extreme fatigue, dyspnea, headache, myalgias, daytime somnolence, difficulty concentrating, loss of taste, loss of smell, tachycardia, and insomnia. He reported that these symptoms were so debilitating that he no longer had the ability to function normally and that it had drastically affected his quality of life.

After discussion with the patient, appropriate informed consent was obtained and a right-sided SGB was performed under fluoroscopic guidance. The stellate ganglion was targeted at the C6 Chassaignac tubercle and, after negative aspiration, a 10-mL treatment mixture consisting of one mL of dexamethasone and 9 mL of 0.25% bupivacaine was injected. Immediately after the procedure, the patient noted a marked improvement in his ability to taste and smell. On postprocedure day one, he endorsed "having the best night of sleep," a noticeable improvement in concentration, decreased headache severity, decreased fatigue, improved appetite, but did not endorse a noticeable improvement in his tachycardia. The patient underwent a left-sided SGB at the same level one week following his initial procedure with the same treatment mixture. On postprocedure day one, the patient stated that his heart rate had returned to baseline and endorsed continued improvement in all of his initial long-COVID symptoms. The patient was subsequently followed in the clinic for 3 months from the initial procedure date and had sustained and near-total relief of all his initial long-COVID symptoms as shown in Table 1 and Fig. 1.

Patient 2

A 55-year-old woman with a past medical history of postherpetic neuralgia presented with dysautonomia that occurred within 2 weeks of her initial COVID-19 infection. Despite resolution of her initial symptoms, she continued to experience fatigue, temperature swings, a sensation of pain in her eyes, inability to smell, sore throat, orthostatic hypotension, tachycardia, loss of appetite, and absence of libido. She stated that these symptoms were so severe and debilitating that they had caused her to become bedridden. She also reported new-onset pseudoseizures, described by the patient as tremors in the bilateral hands and feet in addition to tachycardia, that were triggered by positional changes and stress. The patient was taking multiple medications

Table 1. Long-COVID symptoms over a 3-month period for Patient 1

Scale: 0-10	Initial	After 1st injection	After 2nd injection	After 1 mo	After 2 mos	After 3 mos
Fatigue	10	5	3	1	1	1
Dyspnea	4	2	2	2	0	0
Myalgia	8	5	4	1	1	1
Cough	3	1	1	1	0	0
Headache	7	4	2	0	0	1
Joint pain	0	0	0	0	0	0
Chest pain	0	0	0	0	0	0
Altered smell	9	5	4	1	2	2
Diarrhea	0	0	0	0	0	0
Altered taste	6	3	2	1	0	0

The 0-10 scale used is based on symptom intensity with 10 being the worst intensity of the symptom and 0 being none.

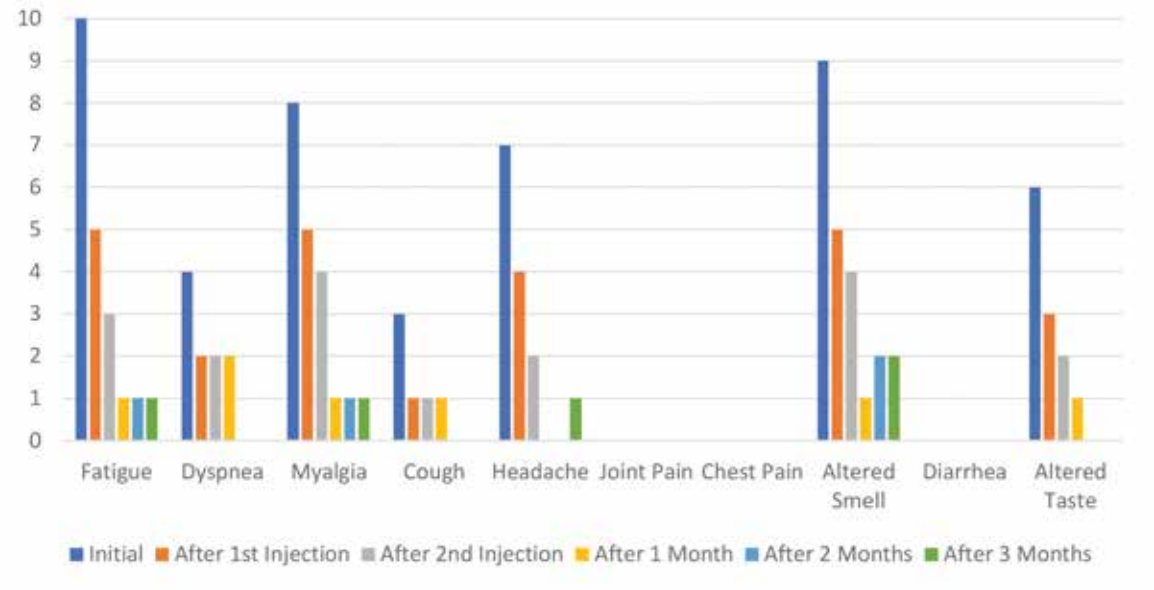

Fig. 1. Graph of long-COVID symptoms in Patient 1 (via symptom intensity on scale of 0-10)

for her symptoms (metoprolol for tachycardia, fludrocortisone for hypotension, omeprazole for acid reflux, and polyethylene glycol for constipation); however, she experienced minimal relief.

After discussion with the patient, appropriate informed consent was obtained and a right-sided SGB was performed at the level of C6 under fluoroscopic guidance, just as with Patient 1. Immediately post procedure, the patient stated that she had regained the ability to smell. One week post procedure, she reported dramatic improvement in all of her initial symptoms and underwent a left-sided SGB at the same level (similar to Patient 1). At one week's follow-up from this procedure, she reported significant improvement in all of her initial symptoms, including her pseudoseizures. At one month's follow-up, the patient revealed that she had sustained a mechanical fall resulting in her hitting her head on the ground, which triggered her prior symptoms of pseudoseizures, orthostatic hypertension, and tachycardia. At this time, we elected to proceed with a radiofrequency ablation (RFA) on her right-sided stellate ganglion (as the left-sided ablation was performed previously). RFA was performed following the same approach described above using a 22-gauge (10-cm, 5-mm active tip) radiofrequency (RF) cannula. Correct positioning was confirmed via injection of contrast medium in the anteroposterior and foraminal oblique views, and precise needle placement was confirmed using sensory (50 Hz, up to 0.8 V) and motor (2 Hz, up to 1.5 V) stimulation. RF lesioning was done at 80°C for 60 seconds, and the patient was monitored closely in the recovery unit for 30 minutes. The patient was subsequently followed in the clinic for 3 months from the initial procedure date and had sustained and near-total relief of all her initial long-COVID symptoms, in addition to resolution of her pseudoseizures, as shown in Table 2 and Fig. 2.

DISCUSSION

The pathogenesis behind many long-COVID symptoms is not well understood, but several mechanisms have been hypothesized including direct viral-mediated neurotoxicity, systemic inflammation, microvascular thrombi, direct virus-mediated cytotoxicity, angiotensin-converting enzyme 2 (ACE2) receptor down-regulation, and immune-mediated inflammation (3). Of specific interest is the hypothesis that the SARS-CoV-2 virus may attach within the autonomic nervous system (ANS) given that long-COVID symptoms can be traced to the ANS and its dysfunction (5). Additionally, autopsy findings have shown evidence of the SARS-CoV-2 virus presence in the brainstem, vagal nerve, glossopharyngeal nerve, and cranial nerves (6). The aforementioned pathomechanisms of attack on the ANS could provide an explanation for autonomic dysfunction due to the sympathovagal imbalance seen in long-COVID patients (7).

Of specific importance is the recent evidence that

Table 2. Long-COVID symptoms over a 3-month period for Patient 2

Scale: 0-10	Initial	After 1st injection	After 2nd injection	After 1 mo	After 2 mos	After 3 mos
Fatigue	9	4	3	2	2	1
Dyspnea	5	4	3	2	2	1
Myalgia	6	4	3	2	2	0
Cough	4	4	4	3	2	0
Headache	6	5	4	2	2	1
Joint pain	0	0	0	0	0	0
Chest pain	0	0	0	0	0	0
Altered smell	7	3	1	1	1	0
Diarrhea	0	0	0	0	0	0
Altered taste	8	4	2	1	1	1

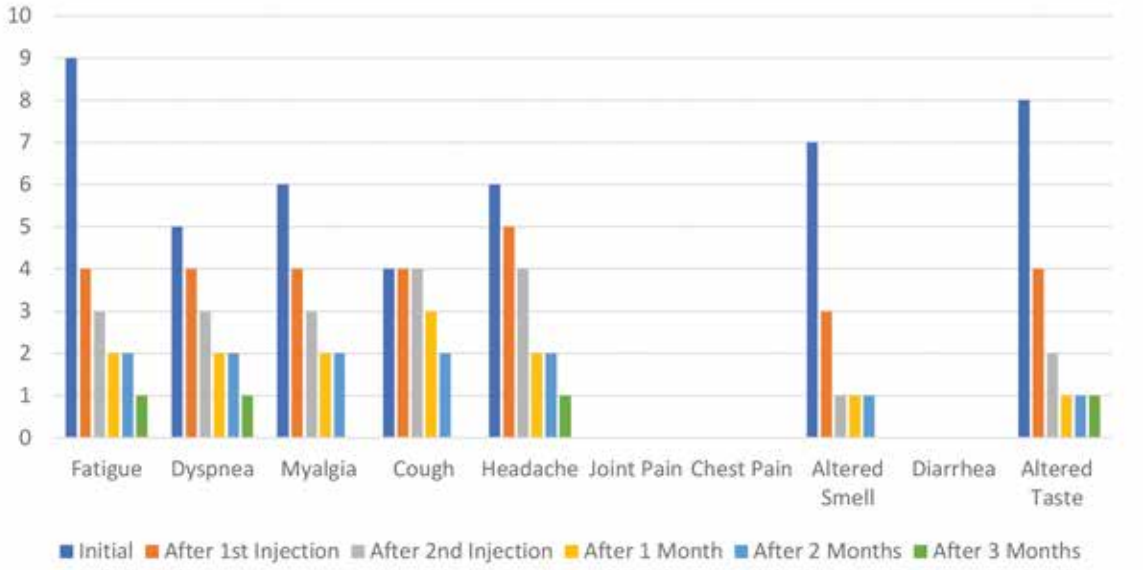

Fig. 2. Graph of long-COVID symptoms in Patient 2 (via symptom intensity on scale of 0-10)

autonomic dysfunction may contribute to long-COVID symptoms that persist beyond acute COVID-19 resolution via findings, in patients with long-COVID, of vagus nerve atrophy and prolonged sympathetic skin response (SSR). The authors discuss the parasympathetic implications accounted for by vagus nerve atrophy and sympathetic implications accounted for by SSR latencies in these patients (8). One can thus postulate that ANS dysfunction leading to sympathovagal imbalance is a possible pathogenic underlying mechanism in long-COVID.

Additionally, it is important to discuss the complex interaction between the ACE2 receptor and COVID-19 as the underlying mechanism behind dysautonomia and its related symptoms (9). Current literature implicates the ACE2 enzyme, which converts angiotensin II (Ang II) to angiotensin (Ang). Ang inhibits inflammation (10). ACE2, expressed in membrane-bound and soluble forms, is the receptor for the spike portion of the SARS-CoV-2 virus. A link between ACE2 and the spike portion of SARS-CoV-2 facilitates the viral entry into the cells while inhibiting the activity of the ACE2 enzyme. A subsequent decrease in the activity of ACE2 potentiates inflammation by perpetuating the feed-forward loop mediated by the Ang II molecule (11). This could lead to dysautonomia induced by the ANS response or maladaptation to pro-inflammatory cytokines leading to excessive sympathetic nervous system activity (12-14).

A recent systematic review on long-COVID found the

10 most common symptoms to be fatigue, dyspnea, myalgia, cough, headache, joint pain, chest pain, altered smell, diarrhea, and altered taste. Additionally, the review found that patients with long-COVID experienced significant negative impacts on their quality of life, mental health, and ability to work in addition to increased risk of multisystem clinical complications (15). For these reasons, and those discussed above, our case series focused on the 10 most common long-COVID symptoms in addition to pertinent impacts related to the patients' lived experience.

A recent case series explored the role of SGB on regional sympathetically mediated dysautonomia in 2 long-COVID patients. The authors discussed augmentation of cerebral blood flow as a possible mechanism for the observed improvements in anosmia and ageusia (4). Although the mechanism by which SGB alleviates long-COVID symptoms is not fully clear, a common hypothesis revolves around the interruption of the central nervous system, specifically the sympathetic nervous system, which allows the body's sympathetic drive to "reset" in a sense. A recent publication focused on the use of SGB to treat the sympathetically driven symptoms of posttraumatic stress disorder discusses this very mechanism, which the authors called "recalibration of regional sympathetic influence" (16) . Our case series further explored the role of SGB in addition to RFA in treating multiple common long-COVID symptoms in both a female and male patient over the longest known follow-up time period to date. Given that the sustained long-COVID symptom relief presented in our case series lasted far longer than the predictable transient sympathetic blockade seen with SGB, further research is necessary to shed light on other possible mechanisms that would explain the sustained and near-complete relief of long-COVID symptoms observed in our patients over 3 months.

CONCLUSION

Our case series presents promising results on the role of SGB in the sustained and near-complete relief of multiple long-COVID symptoms during a 3-month follow-up period. Since the evidence for SGB in treating long-COVID is lacking, we hope this study inspires the initiation of further research and randomized control trials that further explore its role in treating long-COVID symptoms.

Informed Consent Disclosure

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved. The authors state that they have obtained verbal and written informed consent from the patient/patients for the inclusion of their medical and treatment history within this case series.

Author Contributions

OA: This author contributed to the study concept and design, acquisition of data, or analysis and interpretation of data, drafting/revising the manuscript for important intellectual content, and approval of the final version to be published.

MW: This author contributed to the study concept and design, acquisition of data, or analysis and interpretation of data, drafting/revising the manuscript for important intellectual content, and approval of the final version to be published.

SJ: This author contributed to the study concept and design, acquisition of data, or analysis and interpretation of data, drafting/revising the manuscript for important intellectual content, and approval of the final version to be published.

BH: This author contributed to the study concept and design, acquisition of data, or analysis and interpretation of data, drafting/revising the manuscript for important intellectual content, and approval of the final version to be published.

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